UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM

DATE: April 11, 2013

SUBJECT: Demiditraz and Fipronil: Data Evaluation Record for the Study "Determination of Transferable Residues of Demiditraz and Fipronil from the Hair of Dogs Following the Spot-on Treatment Separately with Three Different Formulated End-Use Products"

PC Code: 129121, 577501
MRID No.: 48766704
Petition No.: NA
Assessment Type: Data Evaluation Record
TXR No.: NA

DP Barcode: D400484
Registration No.: NA
Regulatory Action: Risk Assessment
Reregistration Case No.: NA

CAS No.: 120068-37-3, 944263-65-4

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This document serves as a data evaluation record for the demiditraz/fipronil pet residue transfer study, "Determination of Transferable Residues of Demiditraz and Fipronil from the Hair of Dogs Following the Spot-on Treatment Separately with Three Different Formulated End-Use Products (MRID 48766704)," submitted by Pfizer Animal Health in support of the registration of a proposed demiditraz/ fipronil combination dog spot-on product. The study was conducted to measure the amount of demiditraz/ fipronil that may be transferred from dog's hair coat following a single treatment of the spot-on product. A primary review of this study was conducted by Versar, Inc. under the guidance of HED.

STUDY TYPE: Transferable Residues after Gloved Mannequin Hand Contact Simulations to Animal Hair

TEST MATERIAL: The test materials used were three different liquid spot-on formulations:
1) F/PF-03814927+PF-03409397/18, containing 15% demiditraz and 5% fipronil
2) F/PF-03814927+PF-03409397/05, containing 15% demiditraz and 5% fipronil
3) F-PF-03814927+PF-03409397/45, containing 15% demiditraz and 10% fipronil

SYNONYMS:
Demiditraz: 2-[(S)-l-(2,3-Dimethylphenyl)ethyl]-lH-imidazole; CAS 944263-65-4
Fipronil: 5-amino-1-[2,6-dichloro-4-(trifluoromethyl)phenyl]-4-[(trifluoromethyl)sulfinyl]-1*H*-pyrazole-3-carbonitrile; CAS 120068-37-3

CITATION:
Study Author: N. Moorthy Mallipudi, Ph.D.
Title: Determination of Transferable Residues of Demiditraz and Fipronil From the Hair of Dogs Following the Spot-on Treatment Separately with Three Different Formulated End-Use Products
Report Date: February 23, 2012
Performing Laboratories: *In-life phase*:
Eurofins Agroscience Services, Inc.
Sanger, CA, and
Young Veterinary Research Services
Turlock, CA
Analytical phase:
Product Safety Labs (PSL)
Dayton, NJ
Identifying Codes: PSL Study Number 32551; Pfizer Reference Number 1460R-60-11-A79; MRID 48766704

SPONSORS:
Pfizer Animal Health
7000 Portage Road
Kalamazoo, Michigan 49001

EXECUTIVE SUMMARY:

This report reviews the study "Determination of Transferable Residues of Demiditraz and Fipronil From the Hair of Dogs Following the Spot-on Treatment Separately with Three Different Formulated End-Use Products" submitted by Pfizer Animal Health. The purpose of the study was to measure the transferability of the test substance from the hair of a dog through a repeated contact simulation, following a single treatment with a spot-on formulation of demiditraz and fipronil. Three different products were tested, including F/PF-03814927+PF-03409397/18 (Treatment Group I) and F/PF-03814927+PF-03409397/05 (Treatment Group 2) which both contain 15% demiditraz and 5% fipronil; and F-PF-03814927+PF-03409397/45 (Treatment Group 3) which contains 15% demiditraz and 10% fipronil. The nominal application rates were 20 mg of demiditraz/kg bw and 6.7 mg of fipronil/kg bw for

Treatment Groups 1 and 2. The dogs in Treatment Group 3 were treated with half the amount of demiditraz but the same amount of fipronil, that is, 10 mg of demiditraz/kg bw and 6.7 mg of fipronil/kg bw. The test substance was applied directly to the dog's skin at a single site at the base of the neck between the shoulder blades.

A total of 15 beagle dogs were used in the study, including five for each treatment group. Transferred demiditraz and fipronil residues on cotton gloves were measured after 20 repeated contact simulations to the treated dogs. Each simulation consisted of three strokes (60 strokes total) conducted using a mannequin hand fitted with five cotton gloves over top of a nitrile glove. For the pre-application sampling interval, three cotton gloves were placed over the nitrile glove and for the postapplication simulations, five cotton gloves covered the nitrile glove. After the repeated simulations were complete, the gloves were removed individually from the mannequin hand, and the nitrile gloves were discarded. Demiditraz and fipronil residues were extracted from the cotton gloves. Samples were collected from each dog at the following intervals: prior to treatment, at 4 hours (0.17 days) after treatment and at 1, 2, 4, and 7 days after treatment.

Field fortification samples were prepared prior to the application and on the Day 7 sampling interval. Field fortification samples were prepared in triplicate by fortifying glove matrices at 0.01% and 10% of the applied dose for each formulation, resulting in demiditraz fortification levels of 30 and 30,000 µg ai for Treatment Groups I and II and 15 and 15,000 µg ai for Treatment Group 3. Fipronil fortification samples contained 10 and 10,000 µg ai for all treatment groups. Average recoveries by fortification level ranged from 78% to 97%.

Versar calculated individual glove and total residues (sum of the five gloves) in µg/glove, µg/cm^2 of dog surface area, and percent of applied dose transferred. Versar corrected the residues for the average field fortification recovery from the fortification level closest to the field residue. Additionally, residues that were reported as less than the limit of quantitation (LOQ) or as not detected (ND), were assigned a finite value of ½ LOQ for calculation purposes. The limit of detection (LOD) was not reported.

Demiditraz

For all dogs, the outer gloves (Glove #1) contained the highest demiditraz residues as compared to the inner gloves (Glove #2-5). Glove #1 contained between 97 and 99.8% of the total glove residue. Residues declined with each successively inward glove. Residues of demiditraz were less than the LOQ in 13.3% of the innermost glove samples.

Total residues of demiditraz were highest 4 hours after treatment, with an average residue of 7,764 µg/gloves (3.37% of the applied dose or 2.99 µg/cm^2) for Treatment Group 1, 7,533 µg/gloves (2.51% of the applied dose or 2.61 µg/cm^2) for Treatment Group 2, and 4,973 µg/gloves (3.64% of the applied dose or 1.79 µg/cm^2) for Treatment Group 3. Treatment Group 3 dogs received one half the level of demiditraz as that applied to dogs in the other 2 treatment groups. Residues of demiditraz declined over the 7 day sampling interval to 1,679 µg/gloves (0.66% of the applied dose or 0.917 µg/cm^2) for Treatment Group 1, 2,051 µg/gloves (0.684% of the applied dose or 0.700 µg/cm^2) for Treatment Group 2, and 704 µg/gloves (0.50% of the applied dose or 0.251 µg/cm^2) for Treatment Group 3.

Versar assumed first-order dissipation kinetics to generate dissipation curves for the percent of the demiditraz application rate that transferred to the gloves. Versar conducted the linear regression analysis using the natural logarithm of the individual % of applied dose transferred values. Based on linear regression of the natural log transformed data, Versar's calculated half-lives were 2.9 days (R^2 = 0.733) for Treatment Group 1, and 2.3 days (R^2 = 0.727) for Treatment Group 3. The R^2 values were extremely low for Treatment Group 2, indicating a poor fit and therefore a regression is not reported.

The Registrant did not perform a dissipation kinetics analysis.

Fipronil

For all dogs, the outer gloves (Glove #1) contained the highest fipronil residues as compared to the inner gloves (Glove #2-5). Glove #1 contained between 96 and 99.6% of the total glove residue. Residues declined with each successively inward glove. Residues of fipronil were less than the LOQ in 13.5% of the innermost glove samples.

Total residues of fipronil were highest 4 hours after treatment, with average residues of 2,340 µg/gloves (3.06% of the applied dose or 0.903 µg/cm^2) for Treatment Group 1, 2,214 µg/gloves (2.21% of the applied dose or 0.769 µg/cm^2) for Treatment Group 2, and 2,758 µg/gloves (3.03% of the applied dose or 0.988 µg/cm^2) for Treatment Group 3. Residues of fipronil declined over the 7 day sampling interval to 639 µg/gloves (0.75% of the applied dose or 0.235 µg/cm^2) for Treatment Group 1, 772 µg/gloves (0.77% of the applied dose or 0.266 µg/cm^2) for Treatment Group 2, and 898 µg/gloves (0.97% of the applied dose or 0.320 µg/cm^2) for Treatment Group 3.

Versar assumed first-order dissipation kinetics to generate dissipation curves for the percent of the application rate of fipronil that was transferred to cotton gloves. Versar conducted the linear regression analysis using the natural logarithm of the individual % of applied dose transferred values. Based on the regression of the natural log transformed data, Versar's calculated half-lives were 3.3 days ($R^2 = 0.721$) for Treatment Group 1. The regressions for the other 2 treatment groups demonstrated very low R^2 values and half lives are not reported.

The Registrant did not perform a dissipation kinetics analysis.

The following issues of concern are noted:

- No information was provided on the fate of the product once it is applied. The samples were analyzed for parent compounds only.

- Laboratory recovery samples were not prepared. Typically, laboratory fortification samples are performed with each sample run as a check on analytical measurement. The study stated that extra standards were dispersed throughout the sample analyses, along with the regular calibration standards, to make sure the calibration concentrations were accurate.

- The study was conducted using only one breed of dog.

- Field fortification was conducted using two levels, which were expected bracket the anticipated low and high levels of residues from the field (0.01% and 10% of the applied dose). Levels chosen bracketed the majority of residues found on the gloves. The innermost glove samples however, contained residues close to the LOQ which was several orders of magnitude less than the lowest fortification level. For demiditraz, the lowest field fortification level was up to 781x the lowest detectable residue and for fipronil, the lowest field fortification level was up to 312x the lowest detectable residue. A fortification level closer to the LOQ could also have been added to approximate the residues found on these inner glove samples.

- Most of the fipronil and demiditraz residue was detected on the outermost cotton gloves (between 96 and 99.8% of the total glove residue). However, small detectable amounts of residue were found in about 87% of the innermost cotton glove samples (glove #5). The nitrile

glove, which was in between glove #5 and the mannequin hand, was not sampled. Although the USEPA Draft guidance suggests analyzing the chemical resistant gloves, in this case, it is unlikely that any unmeasured residues from the nitrile glove would change the percent of applied dose transferred.

- Two samplers were used for all intervals in order to avoid fatigue, and hence declining technique. The USEPA Draft guidance suggests use of one sampler to ensure consistency.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided. The study sponsor waived claims of confidentiality within the scope of FIFRA Section 10(d) (1) (A), (B), or (C). The study sponsor and director stated that the study was conducted under EPA Good Laboratory Practice Standards (40 CFR part 160) with no exceptions.

CONCURRENT EXPOSURE STUDY: No

WAS AIR SAMPLING CONDUCTED IN CONJUNCTION WITH SURFACE SAMPLING? No

GUIDELINE OR PROTOCOL FOLLOWED: The study was designed according to the US EPA Science Advisory Council for Exposure Draft Guidance Document for Development of Protocols to Collect Pet Fur Transferable Residues Using Mannequin Hands. It was reviewed using using applicable parts of the OCSPP Test Guidelines Series 875, Occupational and Residential Exposure Test Guidelines, Group B: 875.2100 (dislodgeable foliar residue), 875.2300 (indoor surface residue) and 875.2400 (dermal exposure). A compliance checklist is provided in Appendix A.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test Material:

Test material characteristics are provided in Table 1 and Reference Substance characteristics are provided in Table 2.

Table 1: Test Material Characteristics

	Treatment Group I	Treatment Group II	Treatment Group III
Test Substance	F/PF-03814927+PF-03409397/18	F/PF-03814927+PF-03409397/05	F-PF-03814927+PF-03409397/45
Active ingredient	15% demiditraz and 5% fipronil	15% demiditraz and 5% fipronil	15% demiditraz and 10% fipronil
Excipients	γ-hexalactone; 0.8 mEq Laurie Acid; butylhydroxyanisole	n-methylpyrolidone; 0.8 mEq Laurie Acid; butylhydroxyanisole	γ-hexalactone; 0.8 mEq Laurie Acid; butylhydroxyanisole
Lot #	125265/19A	125265/20C	125265/20A
Expiration Date	September 30, 2011	December 31, 2011	July 31, 2011

Table 2: Reference Substance Characteristics

	Demiditraz	Fipronil
Purity	99.6±0.1%	97.5%
Lot #	080031-KQCS	SZBA033XV
CAS #	944263-65-4	120068-37-3

2. Relevance of Test Material to Proposed Formulation(s):

Proposed labels were not provided in the Study Report. The Study Report stated that the products were applied at the intended rates for commercial labels.

B. STUDY DESIGN

The study was conducted according to protocol PSL Study Number 32551, Pfizer Reference Number 1460R-60-11-A79, Determination of Transferable Residues of Demiditraz and Fipronil from the Hair of Dogs Following the Spot-On Treatment Separately with Three Different Formulated End-Use Products, dated June 20, 2011. There were five amendments to the protocol and three deviations from the protocol. The amendments included 1) fixing a typographical error (test substance batch number), 2) using two dogs that were slightly less than 15 pounds (6.8 kg), 3) using volume instead of weight to calculate the actual amount of test substance applied, 4) analyzing both demiditraz and fipronil in the analysis, and 5) auditing the raw data and final study report by the Quality Assurance Unit. The deviations included 1) one sampling event on 4 DAT in Treatment Group 1 was conducted with only 4 gloves instead of 5 gloves, 2) sample storage conditions and researcher's initials were not included on the sampling label, and 3) concurrent fortification samples were not measured. The study reported that the amendments and deviations had no impact on the study.

1. Site Description:

Test location: The study was conducted at the Young Veterinary Research Services facility in Turlock, California. The animals were housed in individual indoor pens.

Meteorological Data: Environmental conditions were monitored using on-site weather monitoring equipment. Air temperature ranged from 61 to 91 °F, and the humidity ranged from 44 to 88%.

2. Animal(s) Monitored:

Species/Breed:	Beagle dogs
Number of animals in study:	15 dogs (4 male and 11 female)
Age:	13 to 62 months old at dose administration
Body weight:	6.1 to 13.8 kg (13.4 to 30.4 lbs) at dose administration

Feeding: According to the study protocol, the maintenance procedures including feeding and access to water were to be recorded in the raw data. The field phase report did not include any information regarding feeding and water access for the dogs.

Health: All of the dogs were in good health and had not been exposed to demiditraz or fipronil for at least 90 days prior to the product application. The dogs had no signs of skin disorders, scrapes, lesions, hair thinning, or any other malady which might have affected the study.

No clinical observations were noted in the dogs that were considered related to the treatment.

No drugs or vaccines were administered during the trial and no animals died during the study.

Surface characteristics: The dogs were bathed with a non-pesticidal shampoo seven days prior to the study and were not bathed again during the study. All dogs had medium hair density and texture with lengths ranging from 1.0 to 2.0 cm.

Other products used: None

3. Physical State of Formulation as Applied:

Spot-on liquid formulation.

4. Application Rates and Regimes:

Application rate(s): The dogs were dosed based on the size of the dog. The nominal dose amounts for the intended commercial labels are shown in Table 3. Dogs in Treatment Group III received one half the amount of demiditraz and the same amount of fipronil as those dogs in Treatment Groups I and II. The nominal application rates were 20 mg of demiditraz/kg and 6.7 mg of fipronil/kg bw for Treatment Groups 1 and 2 (F/PF-03814927+PF-03409397/05 and F-PF-03814927+PF-03409397/45) and 10 mg of demiditraz/kg bw and 6.7 mg of fipronil/kg bw for Treatment Group 3 (F-PF-03814927+PF-03409397/45). The actual amounts of active ingredient applied are provided in Tables 7 and 8.

Table 3. Nominal Dose Amounts

Body Weight of Dog (kg)	Treatment Groups 1 and 2			Treatment Group 3		
	Amount of Formulated End-Use Product Applied (mL)	mg ai Demiditraz	mg ai Fipronil	Amount of Formulated End-Use Product Applied (mL)	mg ai Demiditraz	mg ai Fipronil
3.5-7.5	1	150	50	0.5	75	50
>7.5-15	2	300	100	1.0	150	100
>15-30	5	750	250	2.0	375	250
>30-45	6	900	300	3.0	450	300
>45-60	8	1200	400	4.0	600	400
>60	Appropriate combination of volume			Appropriate combination of volume		

Application Regime: Each of the dogs was treated once at the intended commercial labeled rate. The applicator (YVRS veterinarian) applied the test substance to the dog's skin at the base of the neck, between the shoulder blades. After dispensing, the dog was restrained for approximately one minute and then returned to its individual holding pen.

Application Equipment: The test substance was applied using an animal dosing syringe in which the needle had been discarded after filling the syringe and before application to the dog.

5. Transferable Residue Sampling Procedures:

Method and Equipment: Five cotton gloves (three gloves were used for the pre-application samples) were placed over a powder-free nitrile glove on a mannequin hand. The cotton gloves were dye-free and 100% cotton. Two male mannequin hands, one right and one left, were utilized without prejudice. The mannequin hands were manufactured by Bendies Forms in Quebec, Canada (part number hand 405M). In order to avoid fatigue, and hence declining technique, two samplers performed the repeated simulations. The researchers were randomized to the dogs for each sampling event using the RAND function in Excel.

Sampling Procedure(s): The researcher stroked the body surfaces of the dog with the mannequin hand with a uniform medium pressure and motions. One simulation was comprised of three strokes beginning from the head and ending at the tail base. The three strokes included:

- One stroke on the left side (along the ribcage)
- One stroke on the back line
- One stroke on the right side (along the ribcage)

Contact simulations were conducted using the palmar surface of the gloved mannequin hand, with splayed fingers. Each dog was petted for 20 simulations resulting in a total of 60 strokes. Simulations were performed without regard for the location of the spot-on treatment (i.e. the treatment spot was not avoided during simulations.)

Excessive amounts of hair accumulating on the gloves due to the sampling procedure were removed with care (after completion of the entire simulation).

The cotton gloves were removed one at a time by grasping the glove at the wrist and pulling the glove off the mannequin hand in such a manner as to turn the glove inside out. Each cotton glove sample was placed directly into separate clear glass jars with Teflon® lined lids for storage/extraction resulting in five samples per dog (three for pre-application) per sampling interval. The nitrile glove was discarded after each sampling interval.

Surface area(s) sampled: The total surface area covered by the contact simulation scenario was not provided nor was the palmar surface area of the gloved hand performing the strokes.

Sampling Time: The length of time to complete a single stroke or the entire stroking procedure was not provided.

Replicates per surface:

– Replicates per sampling time: Fifteen dogs were sampled at each interval (5 for each treatment group)

– Number of sampling times: There were a total of 6 sampling intervals, including one sampling event prior to application

Times of sampling: Samples were collected prior to treatment, at 4 hours after treatment, and at 1, 2, 4, and 7 days after treatment.

6. Sample Handling:

After the sampling exercise, each glove sample was placed directly into separate glass jars, capped with Teflon® lined lids, placed into a plastic zipper bag, wrapped in bubble wrap, and then either placed directly into freezers, or stored on dry ice until placed into freezers. Freezer storage temperatures ranged from -20.1 to -28.3°C. Sample storage temperatures were not monitored while on dry ice. Samples were shipped by Federal Express to the analytical laboratory (PSL in East Brunswick, NJ) in ice chests with dry ice on July 12 and July 13, 2011. At the analytical laboratory samples were stored at <-18°C. Samples were stored for a maximum of 58 days prior to analysis.

7. Analytical Methodology:

Extraction method(s): The samples were extracted using methanol:water (1:1, v/v).

Detection method(s): Analysis was performed LC/MS/MS. Table 4 presents a summary of the typical operating conditions.

Table 4. Summary of Chromatographic Operating Conditions

HPLC Conditions		
Column	Phenyl-Hexyl, 50x2.0 mm, 3 µm	
Column temperature	30°C	
Flow Rate	0.4 ml/min	
Mobile phase	A: Water with 0.1% Formic acid; B: Acetonitrile with 0.1% Formic acid	
Injection volume	5 µL	
Retention time	4 to 5 min	
MS Conditions		
Ionization type	Turbo Ion Spray	
Scan Type	MRM	
Polarity	Positive for demiditraz; Negative for fipronil	
Ion transitions	Demiditraz 201.2/95.3 (quantitation) 201.2/133.1 (confirmation)	Fipronil 436.3/331.0 (quantitation) 436.3/400.0 (confirmation)

Method validation: Demiditraz and fipronil residue measurements on cotton glove matrices were analyzed according to the method validated in the study "Development of an Analytical Method for the Determination of Demiditraz and Fipronil in/on Cotton Gloves: Final Report," dated December 20, 2011. The method was verified by fortifying cotton gloves with the three test substances and with dilute solutions of the test substances (prepared in acetonitrile). Recoveries ranged from 91% to 106% for demiditraz and 90% to 111% for fipronil. The limit of quantitation (LOQ) for this method is 0.03 µg per glove for each analyte.

Instrument performance and calibration: A calibration curve with six points was prepared by

injecting constant volumes of calibration standard solutions. The calibration curve was created based on linear regression. The standards ranged from 0.1 to 100 ng/mL.

Quantification: During HPLC analysis, quantitation of residues in all samples was achieved using an external calibration curve calculated by linear regression of instrument responses for the reference substances at multiple concentrations.

8. Quality Control:

Lab Recovery: Laboratory recovery samples were not prepared. Instead, extra standards were dispersed throughout the sample analyses, along with the regular calibration standards, to make sure the calibration concentrations were accurate.

Field blanks: Control glove samples (n=3) were collected from each dog the day prior to application. Residues of demiditraz and fipronil were <LOQ in all samples except for two samples, in which demiditraz was detected at 0.0366 ppm (Treatment Group III, Animal #BEK-0, Glove 1) and fipronil was detected at 0.0551 ppm (Treatment Group III, Animal #DOI-6, Glove 2).

Field recovery: Fortifications were prepared on the day prior to application (June 28, 2011) and on the Day 7 sampling interval (July 6, 2011). Triplicate fortifications were prepared at two levels, 0.01% and 10% of the applied dose for each formulation, resulting in demiditraz fortification levels of 30 and 30,000 µg ai for Treatment Groups I and II and 15 and 15,000 µg ai for Treatment Group III, and fipronil fortification levels of 10 and 10,000 µg ai for all treatment groups. Fortification solution for 0.01% transfer rate was prepared by diluting 0.05 mL of each formulation with 49.95mL of acetonitrile. For the 10% transfer rate treatment, formulations were used as provided. At each fortification event, cotton gloves were placed in glass jars and the fortification solution was placed directly on each glove. After fortification the jars were capped, put in plastic zipper bags and placed into frozen storage. Fortified samples were handled, stored and shipped in the same manner as the residue samples. Field fortification recoveries are summarized in Tables 5 and 6. All of the individual field fortification recoveries were >73%.

Table 5. Field Fortification Recovery for Demiditraz

Interval	Fortification Level (µg/glove)	n	Percent Recovery		
			Recoveries	Average	Standard Deviation
Treatment Group I (F/PF-03814927 + PF-03409397/18)					
Pre-Application	30	3	87, 83, 81	84	3.2
	30,000	3	78, 79,76	78	1.5
Day 7	30	3	93, 87, 79	86	6.9
	30,000	3	87, 79, 82	83	4.1
Overall	30	6	79-83	**85**	5.0
	30,000	6	76-87	**80**	3.9
Treatment Group II (F/PF-03814927 + PF-03409397/05)					
Pre-Application	30	3	91, 89, 165[1]	90	NA
	30,000	3	73, 80, 81	78	4.2
Day 7	30	3	90, 92, 91	91	0.8

Table 5. Field Fortification Recovery for Demiditraz					
Interval	Fortification Level (µg/glove)	n	Percent Recovery		
			Recoveries	Average	Standard Deviation
	30,000	3	85, 77, 76	79	4.9
Overall	30	6	89-165	**91**	1.0
	30,000	6	73-85	**78**	4.1
Treatment Group III (F/PF-03814927 + PF-03409397/45)					
Pre-Application	15	3	91, 89, 88	90	1.7
	15,000	3	99, 97, 99	98	0.8
Day 7	15	3	88, 83, 81	84	3.8
	15,000	3	91, 93, 93	92	0.8
Overall	15	6	81-91	**87**	4.1
	15,000	6	91-99	**95**	3.4

[1]The study author suspects that this glove might have been fortified twice by error. The value was not included in the average recovery calculations.

Table 6. Field Fortification Recovery for Fipronil					
Interval	Fortification Level (µg/glove)	n	Percent Recovery		
			Recoveries	Average	Standard Deviation
Treatment Group I (F/PF-03814927 + PF-03409397/18)					
Pre-Application	10	3	91, 85, 89	88	2.9
	10,000	3	94, 94, 95	95	0.5
Day 7	10	3	94, 90, 85	90	4.5
	10,000	3	110, 93, 97	100	8.7
Overall	10	6	85-94	**89**	3.5
	10,000	6	93-110	**97**	6.3
Treatment Group II (F/PF-03814927 + PF-03409397/05)					
Pre-Application	10	3	96, 96, 186[1]	96	NA
	10,000	3	90, 93, 95	93	2.9
Day 7	10	3	97, 95, 92	95	2.6
	10,000	3	102, 93, 92	96	5.5
Overall	10	6	92-186	**95**	1.9
	10,000	6	90-102	**94**	4.3
Treatment Group III (F/PF-03814927 + PF-03409397/45)					
Pre-Application	10	3	91, 93, 90	91	1.8
	10,000	3	97, 97, 97	97	0.4
Day 7	10	3	90, 89, 87	89	1.9
	10,000	3	90, 96, 95	93	3.3
Overall	10	6	87-93	**90**	2.2
	10,000	6	90-97	**95**	2.8

[1]The study author suspects that this glove might have been fortified twice by error. The value was not included in the average recovery calculations.

Formulation: Three different spot-on products were tested, including F/PF-03814927+PF-03409397/18 and F/PF-03814927+PF-03409397/05 which both contain 15% demiditraz and 5% fipronil, and F-PF-03814927+ PF-03409397/45 which

contains 15% demiditraz and 10% fipronil.

Tank mix: Not applicable.

Travel Recovery: Travel recovery samples were not prepared.

Storage Stability: Storage stability was not conducted; however, field fortification samples demonstrated the stability of demiditraz and fipronil in cotton gloves for the storage duration.

II. RESULTS AND CALCULATIONS

Measured residues (µg/gloves) detected in each glove sample (outer plus 4 inner cotton gloves) are shown in Tables 7 and 8 for demiditraz and fipronil. The study reviewer corrected the residues for the average field fortification recovery from the fortification level closest to the field residue (refer to Tables 5 and 6). Additionally, residues that were reported as less than the LOQ or as ND, were assigned a finite value of ½ LOQ for calculation purposes. The study reviewer also calculated total residues (sum of 5 gloves samples per dog) in µg/glove and µg/cm^2 of dog surface area, as well as the percent of applied dose transferred. These values are shown per dog in Tables 7 and 8, and are also summarized in Tables 9 and 10. The Registrant only provided measured residues on a per sample basis, in µg/glove and as the percent of applied dose transferred to each glove. The Registrant did not correct the residues for field fortification recoveries.

The surface area of the dog was determined using the following equation:

$$\textit{Surface area of dog (cm}^2\textit{)} = (12.3*((\textit{animal body weight (lbs)}*454)^{0.65}))$$

Demiditraz

For all dogs, the outer gloves (Glove #1) contained the highest demiditraz residues as compared to the inner gloves (Glove #2-5). Glove #1 contained between 97 and 99.8% of the total glove residue. Residues determined on gloves declined with each successively inward glove. Residues of demiditraz were less than the LOQ in approximately 13% of the innermost glove samples.

Total residues of demiditraz were highest 4 hours after treatment, with an average residue of 7,764 µg/gloves (3.37% of the applied dose or 2.99 µg/cm^2) for Treatment Group 1, 7,533 µg/gloves (2.51% of the applied dose or 2.61 µg/cm^2) for Treatment Group 2, and 4,973 µg/gloves (3.64% of the applied dose or 1.79 µg/cm^2) for Treatment Group 3. Treatment Group 3 dogs received one half the level of demiditraz as that applied to dogs in the other 2 treatment groups. Residues of demiditraz declined over the 7 day sampling interval to 1,679 µg/gloves (0.66% of the applied dose or 0.917 µg/cm^2) for Treatment Group 1, 2,051 µg/gloves (0.684% of the applied dose or 0.700 µg/cm^2) for Treatment Group 2, and 704 µg/gloves (0.50% of the applied dose or 0.251 µg/cm^2) for Treatment Group 3.

Versar assumed first-order dissipation kinetics to generate dissipation curves for the percent of the demiditraz application rate that transferred to the gloves. Versar conducted the linear regression analysis using the natural logarithm of the individual % of applied dose transferred values. Based on linear regression of the natural log transformed data, Versar's calculated half-lives were 2.9 days (R^2 = 0.733) for Treatment Group 1, and 2.3 days (R^2 = 0.727) for Treatment Group 3. The R^2 values were extremely low for Treatment Group 2, indicating a poor fit and therefore a regression is not reported.

The Registrant did not perform a dissipation kinetics analysis.

Fipronil

For all dogs, the outer gloves (Glove #1) contained the highest fipronil residues as compared to the inner gloves (Glove #2-5). Glove #1 contained between 96 and 99.6% of the total glove residue. Residues declined with each successively inward glove. Residues of fipronil were less than the LOQ in approximately 13% of the innermost glove samples.

Total residues of fipronil were highest 4 hours after treatment, with average residues of 2,340 µg/gloves (3.06% of the applied dose or 0.903 µg/cm^2) for Treatment Group 1, 2,214 µg/gloves (2.21% of the applied dose or 0.769 µg/cm^2) for Treatment Group 2, and 2,758 µg/gloves (3.03% of the applied dose or 0.988 µg/cm^2) for Treatment Group 3. Residues of fipronil declined over the 7 day sampling interval to 639 µg/gloves (0.75% of the applied dose or 0.235 µg/cm^2) for Treatment Group 1, 772 µg/gloves (0.77% of the applied dose or 0.266 µg/cm^2) for Treatment Group 2, and 898 µg/gloves (0.97% of the applied dose or 0.320 µg/cm^2) for Treatment Group 3.

Versar assumed first-order dissipation kinetics to generate dissipation curves for the percent of the fipronil application rate that transferred to the gloves. Versar conducted the linear regression analysis using the natural logarithm of the individual % of applied dose transferred values. Based on linear regression of the natural log transformed data, Versar's calculated half life was 3.3 days ($R^2 = 0.721$) for Treatment Group 1. The regressions for the other 2 treatment groups demonstrated very low R^2 values and half lives are not reported.

The Registrant did not perform a dissipation kinetics analysis.

III. DISCUSSION

A. LIMITATIONS OF THE STUDY:

The following issues of concern are noted:

- No information was provided on the fate of the product once it is applied. The samples were analyzed for parent compounds only.
- Laboratory recovery samples were not prepared. Typically, laboratory fortification samples are performed with each sample run as a check on analytical measurement. The study stated that extra standards were dispersed throughout the sample analyses, along with the regular calibration standards, to make sure the calibration concentrations were accurate.
- The study was conducted using only one breed of dog.
- Field fortification was conducted using two levels, which were expected bracket the anticipated low and high levels of residues from the field (0.01% and 10% of the applied dose). Levels chosen bracketed the majority of residues found on the gloves. The innermost glove samples however, contained residues close to the LOQ which was several orders of magnitude less than the lowest fortification level. For demiditraz, the lowest field fortification level was up to 781x the lowest detectable residue and for fipronil, the lowest field fortification level was up to 312x the lowest detectable residue. A fortification level closer to the LOQ could also have been added to approximate the residues found on these inner glove samples.

- Most of the fipronil and demiditraz residue was detected on the outermost cotton gloves (between 96 and 99.8% of the total glove residue). However, small detectable amounts of residue were found in about 87% of the innermost cotton glove samples (glove #5). The nitrile glove, which was in between glove #5 and the mannequin hand, was not sampled. Although the USEPA Draft guidance suggests analyzing the chemical resistant gloves, in this case, it is unlikely that any unmeasured residues from the nitrile glove would change the percent of applied dose transferred.

- Two samplers were used for all intervals in order to avoid fatigue, and hence declining technique. The USEPA Draft guidance suggests use of one sampler to ensure consistency.

B. CONCLUSIONS:

The Registrant and Versar calculated similar transferable residues. The slight differences are most likely due to Versar's use of ½ LOD or ½ LOQ for those values assayed at less than the LOD or LOQ. The Registrant reported total residues as the sum of detectable residues on each glove.

Table 7. Demiditraz Residues from Cotton Gloves Following 20 Contact Simulations to Treated Dogs[1]

Interval	Animal #	Animal Weight (kg)	Animal Surface Area (cm^2)	Actual Dose Applied (µg ai)	Measured Residue on Gloves (µg/glove)[2, 3]					Total Residue		% of applied dose transferred[6]
					Outer Cotton Glove #1	Inner Cotton Glove #2	Inner Cotton Glove #3	Inner Cotton Glove #4	Inner Cotton Glove #5	µg/gloves[4]	µg/cm^2 surface area of dog[5]	
Treatment Group 1 (F/PF-03814927 + PF-03409397/18)												
Pre-Application	CRK-0	6.1	2,125	0	ND	ND	ND	Not sampled		--	--	--
	TXJ-6	11.7	3,246	0	ND	<LOQ	ND	Not sampled		--	--	--
	IAK-0	6.7	2,259	0	ND	ND	ND	Not sampled		--	--	--
	GGK-0	8.3	2,597	0	ND	<LOQ	ND	Not sampled		--	--	--
	FSK-0	9.2	2,776	0	ND	<LOQ	ND	Not sampled		--	--	--
4 hours	CRK-0	6.1	2,125	150,000	5,565	24.8	1.31	0.155	<LOQ	5,591	2.63	3.73
	TXJ-6	11.7	3,246	300,000	8,141	14.5	1.66	0.540	0.212	8,158	2.51	2.72
	IAK-0	6.7	2,259	150,000	6,094	8.72	1.60	0.228	0.0824	6,105	2.70	4.07
	GGK-0	8.3	2,597	300,000	10,694	29.6	1.13	0.253	0.109	10,725	4.13	3.58
	FSK-0	9.2	2,776	300,000	8,212	21.9	4.31	0.833	0.316	8,239	2.97	2.75
Day 1	CRK-0	6.1	2,125	150,000	3,847	19.1	0.741	0.100	<LOQ	3,867	1.82	2.58
	TXJ-6	11.7	3,246	300,000	6,094	30.7	1.13	0.225	0.627	6,127	1.89	2.04
	IAK-0	6.7	2,259	150,000	3,812	20.4	0.501	0.586	<LOQ	3,833	1.70	2.56
	GGK-0	8.3	2,597	300,000	6,565	48.2	1.48	0.568	0.691	6,616	2.55	2.21
	FSK-0	9.2	2,776	300,000	5,153	58.5	2.72	0.487	0.102	5,215	1.88	1.74
Day 2	CRK-0	6.1	2,125	150,000	2,200	17.5	0.61	0.097	<LOQ	2,218	1.04	1.48
	TXJ-6	11.7	3,246	300,000	4,482	76.6	5.68	1.306	0.360	4,566	1.41	1.52
	IAK-0	6.7	2,259	150,000	1,976	18.6	1.46	0.265	0.0546	1,997	0.884	1.33
	GGK-0	8.3	2,597	300,000	6,918	89.9	4.69	3.376	0.948	7,017	2.70	2.34
	FSK-0	9.2	2,776	300,000	3,494	49.1	2.46	0.519	0.142	3,546	1.28	1.18
Day 4	CRK-0	6.1	2,125	150,000	1,329	7.88	0.553	0.126	ND	1,338	0.630	0.89
	TXJ-6	11.7	3,246	300,000	4,765	61.3	7.12	1.682	0.289	4,835	1.49	1.61

Table 7. Demiditraz Residues from Cotton Gloves Following 20 Contact Simulations to Treated Dogs[1]

Interval	Animal #	Animal Weight (kg)	Animal Surface Area (cm^2)	Actual Dose Applied (µg ai)	Measured Residue on Gloves (µg/glove)[2, 3]					Total Residue		% of applied dose transferred[6]
					Outer Cotton Glove #1	Inner Cotton Glove #2	Inner Cotton Glove #3	Inner Cotton Glove #4	Inner Cotton Glove #5	µg/gloves[4]	µg/cm^2 surface area of dog[5]	
	IAK-0	6.7	2,259	150,000	882	7.58	0.452	0.065	No sample	890	0.394	0.59
	GGK-0	8.3	2,597	300,000	4,200	45.9	3.94	0.593	1.38	4,252	1.64	1.42
	FSK-0	9.2	2,776	300,000	1,188	0.214	12.9	1.388	0.189	1,203	0.433	0.40
Day 7	CRK-0	6.1	2,125	150,000	778	3.53	ND	<LOQ	<LOQ	781	0.368	0.52
	TXJ-6	11.7	3,246	300,000	2,635	39.9	4.26	1.101	0.239	2,681	0.826	0.89
	IAK-0	6.7	2,259	150,000	720	4.69	0.359	0.039	0.0572	725	0.321	0.48
	GGK-0	8.3	2,597	300,000	2,824	29.9	3.07	0.709	0.156	2,857	1.10	0.95
	FSK-0	9.2	2,776	300,000	1,329	19.8	1.01	0.111	0.0452	1,350	0.486	0.45

Table 7. Demiditraz Residues from Cotton Gloves Following 20 Contact Simulations to Treated Dogs[1]

Interval	Animal #	Animal Weight (kg)	Animal Surface Area (cm^2)	Actual Dose Applied (µg ai)	Measured Residue on Gloves (µg/glove)[2, 3]					Total Residue		% of applied dose transferred[6]
					Outer Cotton Glove #1	Inner Cotton Glove #2	Inner Cotton Glove #3	Inner Cotton Glove #4	Inner Cotton Glove #5	µg/gloves[4]	µg/cm^2 surface area of dog[5]	
Treatment Group 2 (F/PF-03814927 + PF-03409397/05)												
Pre-Application	QUI-6	9.8	2,893	0	ND	<LOQ	ND	Not sampled		--	--	--
	UHJ-6	9.6	2,854	0	ND	<LOQ	ND	Not sampled		--	--	--
	BAI-6	8.8	2,697	0	ND	<LOQ	ND	Not sampled		--	--	--
	KZI-6	9	2,737	0	ND	ND	ND	Not sampled		--	--	--
	LKJ-6	13.8	3,613	0	ND	<LOQ	ND	Not sampled		--	--	--
4 hours	QUI-6	9.8	2,893	300,000	7,374	24.3	1.31	0.464	0.0959	7,400	2.56	2.47
	UHJ-6	9.6	2,854	300,000	8,725	51.0	3.62	0.437	0.114	8,780	3.08	2.93
	BAI-6	8.8	2,697	300,000	7,769	64.6	3.07	0.501	0.157	7,838	2.91	2.61
	KZI-6	9	2,737	300,000	8,297	78.1	4.52	1.43	0.226	8,381	3.06	2.79
	LKJ-6	13.8	3,613	300,000	5,242	21.0	0.903	0.0969	***0.015***	5,264	1.46	1.75
Day 1	QUI-6	9.8	2,893	300,000	2,209	21.6	0.989	0.230	0.107	2,232	0.772	0.74
	UHJ-6	9.6	2,854	300,000	3,813	42.5	2.66	0.379	0.158	3,859	1.35	1.29
	BAI-6	8.8	2,697	300,000	2,132	34.8	3.05	0.629	0.168	2,171	0.805	0.72
	KZI-6	9	2,737	300,000	2,407	46.8	4.95	0.204	0.0696	2,459	0.898	0.82
	LKJ-6	13.8	3,613	300,000	2,264	23.0	1.24	14.1	***0.015***	2,302	0.637	0.77
Day 2	QUI-6	9.8	2,893	300,000	1,813	22.0	3.23	0.889	0.230	1,840	0.636	0.61
	UHJ-6	9.6	2,854	300,000	3,824	43.4	1.97	0.359	0.133	3,870	1.36	1.29
	BAI-6	8.8	2,697	300,000	1,407	35.5	4.01	0.340	0.991	1,447	0.537	0.48
	KZI-6	9	2,737	300,000	2,571	48.8	4.31	0.785	0.368	2,626	0.959	0.88
	LKJ-6	13.8	3,613	300,000	1,143	24.9	1.34	0.067	0.333	1,170	0.324	0.39
Day 4	QUI-6	9.8	2,893	300,000	2,033	22.0	2.44	1.495	0.195	2,059	0.712	0.69
	UHJ-6	9.6	2,854	300,000	3,154	39.1	2.41	0.966	0.144	3,196	1.120	1.07
	BAI-6	8.8	2,697	300,000	1,736	33.8	4.29	7.31	0.0955	1,782	0.661	0.59
	KZI-6	9	2,737	300,000	2,571	56.6	7.12	3.46	1.626	2,640	0.965	0.88
	LKJ-6	13.8	3,613	300,000	2,077	28.9	1.37	1.07	0.0375	2,108	0.583	0.70
Day 7	QUI-6	9.8	2,893	300,000	2,011	28.9	2.73	0.231	0.100	2,043	0.706	0.68
	UHJ-6	9.6	2,854	300,000	1,802	24.6	3.36	0.546	0.0982	1,831	0.641	0.61
	BAI-6	8.8	2,697	150,000	1,835	31.3	5.74	0.735	0.168	1,873	0.694	0.62
	KZI-6	9	2,737	300,000	2,308	65.8	6.68	1.95	0.378	2,383	0.871	0.79
	LKJ-6	13.8	3,613	300,000	2,066	58.9	2.10	0.696	0.266	2,128	0.589	0.71
Treatment Group 3 (F-PF-03814927 + PF-03409397/45)												
Pre-Application	LGJ-6	12.4	3,371	0	ND	<LOQ	ND	Not sampled		--	--	--
	DOI-6	8.2	2,576	0	ND	<LOQ	ND	Not sampled		--	--	--
	CQI-6	8.7	2,677	0	ND	<LOQ	ND	Not sampled		--	--	--
	BEK-0	6.9	2,303	0	0.0366	ND	ND	Not sampled		--	--	--
	PLI-6	10.3	2,988	0	ND	ND	ND	Not sampled		--	--	--

Table 7. Demiditraz Residues from Cotton Gloves Following 20 Contact Simulations to Treated Dogs[1]

Interval	Animal #	Animal Weight (kg)	Animal Surface Area (cm^2)	Actual Dose Applied (µg ai)	Measured Residue on Gloves (µg/glove)[2, 3]					Total Residue		% of applied dose transferred[6]
					Outer Cotton Glove #1	Inner Cotton Glove #2	Inner Cotton Glove #3	Inner Cotton Glove #4	Inner Cotton Glove #5	µg/gloves[4]	µg/cm^2 surface area of dog[5]	
4 hours	LGJ-6	12.4	3,371	150,000	4,724	45.5	1.37	0.471	0.134	4,772	1.42	3.18
	DOI-6	8.2	2,576	150,000	5,161	24.7	1.23	0.399	0.213	5,187	2.01	3.46
	CQI-6	8.7	2,677	150,000	6,862	58.6	1.90	0.275	0.0692	6,923	2.59	4.62
	BEK-0	6.9	2,303	75,000	2,379	27.6	1.67	0.220	0.0455	2,409	1.05	3.21
	PLI-6	10.3	2,988	150,000	5,437	125	10.3	1.425	0.361	5,574	1.87	3.72
Day 1	LGJ-6	12.4	3,371	150,000	3,057	23.1	0.921	0.169	0.0448	3,082	0.914	2.05
	DOI-6	8.2	2,576	150,000	3,437	26.6	1.43	0.354	0.437	3,466	1.35	2.31
	CQI-6	8.7	2,677	150,000	2,897	65.9	3.55	0.871	0.155	2,967	1.11	1.98
	BEK-0	6.9	2,303	75,000	1,632	37.1	1.20	0.224	<LOQ	1,671	0.726	2.23
	PLI-6	10.3	2,988	150,000	3,931	67.6	2.41	0.459	0.103	4,002	1.34	2.67
Day 2	LGJ-6	12.4	3,371	150,000	1,299	23.4	1.95	0.930	0.230	1,325	0.393	0.88
	DOI-6	8.2	2,576	150,000	1,816	20.9	2.06	0.652	0.838	1,841	0.714	1.23
	CQI-6	8.7	2,677	150,000	1,287	15.5	1.11	0.217	0.0820	1,304	0.487	0.87
	BEK-0	6.9	2,303	75,000	638	16.9	0.744	0.168	0.0485	656	0.285	0.87
	PLI-6	10.3	2,988	150,000	3,069	37.1	1.099	0.999	0.540	3,109	1.041	2.07
Day 4	LGJ-6	12.4	3,371	150,000	828	13.9	1.61	0.392	0.230	844	0.250	0.56
	DOI-6	8.2	2,576	150,000	1,057	14.9	1.06	0.528	0.157	1,074	0.417	0.72
	CQI-6	8.7	2,677	150,000	409	9.61	0.572	0.654	0.126	420	0.157	0.28
	BEK-0	6.9	2,303	75,000	300	5.69	0.548	0.092	0.0375	306	0.133	0.41
	PLI-6	10.3	2,988	150,000	1,147	42.6	6.51	0.920	0.362	1,198	0.401	0.80
Day 7	LGJ-6	12.4	3,371	150,000	510	10.5	1.66	0.345	0.0813	523	0.155	0.35
	DOI-6	8.2	2,576	150,000	1,055	1.85	1.33	0.271	0.368	1,059	0.411	0.71
	CQI-6	8.7	2,677	150,000	324	8.62	0.659	0.178	0.0679	334	0.125	0.22
	BEK-0	6.9	2,303	75,000	261	4.47	0.282	0.058	0.0592	266	0.115	0.35
	PLI-6	10.3	2,988	150,000	1,310	24.5	0.606	0.426	0.378	1,336	0.447	0.89

1. **Nominal application rates were :**
   20 mg of demiditraz/kg and 6.7 mg of fipronil/kg bw for Treatment Groups 1 and 2
   10 mg of demiditraz/kg bw and 6.7 mg of fipronil/kg bw for Treatment Group 3.
2. Residues were corrected for field fortification recovery using the average percent recovery from the fortification level closest to the field residue.
   Treatment Group 1: 85% for residues <15,015 µg/sample and 80% for residues ≥15,015 µg/sample
   Treatment Group 2: 91% for residues <15,015 µg/sample and 78% for residues ≥15,015 µg/sample
   Treatment Group 3: 87% for residues <7,508 µg/sample and 95% for residues ≥7,508 µg/sample
3. LOQ = 0.03 µg/glove. ND = Not detected (no peak). LOD was not provided. When residues were reported as less than the LOQ or ND, Versar used a value of ½ LOQ (0.015 µg/glove) in the calculations.
4. Total Residue (µg/gloves) = outer cotton glove #1 + inner glove #2 + inner glove #3 (µg/glove) + inner glove #4 (µg/glove) + inner glove #5 (µg/glove).
5. Total Residue (µg/cm^2) = Total residue on all 5 gloves / cm^2 body surface area of the dog.
6. % of applied dose transferred = Total Residue (µg/gloves) / applied dose (µg ai) *100

Note: One simulation = 60 strokes

Table 8. Fipronil Residues from Cotton Gloves Following 20 Contact Simulations to Treated Dogs[1]

Interval	Animal #	Animal Weight (kg)	Animal Surface Area (cm^2)	Actual Dose Applied (µg ai)	Measured Residue on Gloves (µg/glove)[2, 3]					Total Residue		% of applied dose transferred[6]
					Outer Cotton Glove #1	Inner Cotton Glove #2	Inner Cotton Glove #3	Inner Cotton Glove #4	Inner Cotton Glove #5	µg/gloves[4]	µg/cm^2 surface area of dog[5]	
Treatment Group 1 (F/PF-03814927 + PF-03409397/18)												
Pre-Application	CRK-0	6.1	2,125	0	ND	ND	ND	Not sampled		--	--	--
	TXJ-6	11.7	3,246	0	ND	ND	ND	Not sampled		--	--	--
	IAK-0	6.7	2,259	0	ND	ND	ND	Not sampled		--	--	--
	GGK-0	8.3	2,597	0	ND	ND	ND	Not sampled		--	--	--
	FSK-0	9.2	2,776	0	<LOQ	ND	ND	Not sampled		--	--	--
4 hours	CRK-0	6.1	2,125	50,000	1,843	7.87	0.512	0.054	<LOQ	1,851	0.871	3.70
	TXJ-6	11.7	3,246	100,000	2,393	11.3	0.556	0.212	0.0640	2,405	0.741	2.41
	IAK-0	6.7	2,259	50,000	1,719	6.37	0.613	0.0902	<LOQ	1,726	0.764	3.45
	GGK-0	8.3	2,597	100,000	3,258	23.9	0.431	0.107	0.0481	3,283	1.26	3.28
	FSK-0	9.2	2,776	100,000	2,416	16.7	1.71	0.322	0.0991	2,435	0.877	2.43
Day 1	CRK-0	6.1	2,125	50,000	1,371	6.18	0.281	0.0619	<LOQ	1,377	0.648	2.75
	TXJ-6	11.7	3,246	100,000	1,888	11.3	0.545	0.109	0.260	1,900	0.585	1.90
	IAK-0	6.7	2,259	50,000	1,382	6.29	0.233	0.303	<LOQ	1,389	0.615	2.78
	GGK-0	8.3	2,597	100,000	2,191	15.8	0.690	0.300	0.287	2,208	0.850	2.21
	FSK-0	9.2	2,776	100,000	1,685	17.4	1.19	0.216	0.0838	1,704	0.614	1.70
Day 2	CRK-0	6.1	2,125	50,000	919	6.97	0.281	0.0700	<LOQ	926	0.436	1.85
	TXJ-6	11.7	3,246	100,000	1,618	27.5	1.98	0.535	0.204	1,648	0.508	1.65
	IAK-0	6.7	2,259	50,000	816	6.46	0.639	0.124	0.0430	823	0.364	1.65
	GGK-0	8.3	2,597	100,000	2,652	26.5	1.89	1.079	0.525	2,682	1.03	2.68
	FSK-0	9.2	2,776	100,000	1,180	14.2	0.875	0.215	0.0747	1,195	0.430	1.20
Day 4	CRK-0	6.1	2,125	50,000	528	3.37	0.303	0.235	ND	532	0.250	1.06
	TXJ-6	11.7	3,246	100,000	1,596	19.1	2.39	0.687	0.137	1,618	0.498	1.62
	IAK-0	6.7	2,259	50,000	448	2.75	0.209	0.0492	ND	451	0.200	0.90
	GGK-0	8.3	2,597	100,000	1,663	15.4	1.47	0.292	0.617	1,681	0.647	1.68
	FSK-0	9.2	2,776	100,000	478	0.290	5.11	0.549	0.0883	484	0.174	0.48
Day 7	CRK-0	6.1	2,125	50,000	285	1.3	ND	0.204	No sample	287	0.135	0.57
	TXJ-6	11.7	3,246	100,000	1,045	12.6	1.71	0.319	0.128	1,060	0.326	1.06
	IAK-0	6.7	2,259	50,000	262	1.53	0.140	0.0371	0.0380	264	0.117	0.53
	GGK-0	8.3	2,597	100,000	1,075	10.1	1.47	0.363	0.0944	1,087	0.419	1.09
	FSK-0	9.2	2,776	100,000	492	5.65	0.411	0.0725	0.0360	498	0.179	0.50
Treatment Group 2 (F/PF-03814927 + PF-03409397/05)												
Pre-Application	QUI-6	9.8	2,893	0	ND	ND	ND	Not sampled		--	--	--
	UHJ-6	9.6	2,854	0	ND	ND	ND	Not sampled		--	--	--
	BAI-6	8.8	2,697	0	ND	ND	ND	Not sampled		--	--	--
	KZI-6	9	2,737	0	ND	ND	ND	Not sampled		--	--	--
	LKJ-6	13.8	3,613	0	ND	ND	ND	Not sampled		--	--	--

Table 8. Fipronil Residues from Cotton Gloves Following 20 Contact Simulations to Treated Dogs[1]													
Interval	Animal #	Animal Weight (kg)	Animal Surface Area (cm^2)	Actual Dose Applied (µg ai)	Measured Residue on Gloves (µg/glove)[2, 3]					Total Residue		% of applied dose transferred[6]
					Outer Cotton Glove #1	Inner Cotton Glove #2	Inner Cotton Glove #3	Inner Cotton Glove #4	Inner Cotton Glove #5	µg/gloves[4]	µg/cm^2 surface area of dog[5]	
4 hours	QUI-6	9.8	2,893	100,000	2,274	8.05	0.733	0.248	0.0507	2,283	0.789	2.28
	UHJ-6	9.6	2,854	100,000	2,579	17.7	1.99	0.287	0.0640	2,599	0.911	2.60
	BAI-6	8.8	2,697	100,000	2,295	21.1	1.93	0.334	0.111	2,318	0.859	2.32
	KZI-6	9	2,737	100,000	2,400	26.7	2.93	0.871	0.121	2,431	0.888	2.43
	LKJ-6	13.8	3,613	100,000	1,432	6.81	0.665	0.0622	<LOQ	1,439	0.398	1.44
Day 1	QUI-6	9.8	2,893	100,000	1,263	11.9	0.637	0.155	0.0675	1,276	0.441	1.28
	UHJ-6	9.6	2,854	100,000	2,232	23.4	1.63	0.199	0.0957	2,257	0.791	2.26
	BAI-6	8.8	2,697	100,000	1,147	18.3	1.76	0.318	0.0941	1,168	0.433	1.17
	KZI-6	9	2,737	100,000	1,347	26.2	2.86	0.580	0.227	1,377	0.503	1.38
	LKJ-6	13.8	3,613	100,000	659	6.73	0.545	7.35	<LOQ	674	0.186	0.67
Day 2	QUI-6	9.8	2,893	100,000	1,126	11.7	1.93	0.571	0.152	1,141	0.394	1.14
	UHJ-6	9.6	2,854	100,000	2,400	24.8	1.41	0.274	0.0808	2,427	0.850	2.43
	BAI-6	8.8	2,697	100,000	953	20.4	2.48	0.223	0.600	976	0.362	0.98
	KZI-6	9	2,737	100,000	1,579	25.5	2.61	0.492	0.214	1,608	0.587	1.61
	LKJ-6	13.8	3,613	100,000	663	11.3	0.74	0.103	0.196	675	0.187	0.68
Day 4	QUI-6	9.8	2,893	100,000	817	7.39	1.01	0.429	0.0603	826	0.285	0.83
	UHJ-6	9.6	2,854	100,000	1,284	15.6	1.04	0.325	0.0559	1,301	0.456	1.30
	BAI-6	8.8	2,697	100,000	656	11.2	1.54	2.43	0.0340	671	0.249	0.67
	KZI-6	9	2,737	100,000	921	18.0	2.48	1.24	0.523	943	0.345	0.94
	LKJ-6	13.8	3,613	100,000	726	8.78	0.417	0.189	<LOQ	736	0.204	0.74
Day 7	QUI-6	9.8	2,893	100,000	766	9.35	1.05	0.079	0.0404	777	0.269	0.78
	UHJ-6	9.6	2,854	100,000	773	9.78	1.55	0.227	0.0435	784	0.275	0.78
	BAI-6	8.8	2,697	100,000	698	11.1	2.04	0.275	0.0534	711	0.264	0.71
	KZI-6	9	2,737	100,000	889	21.5	2.53	0.726	0.125	914	0.334	0.91
	LKJ-6	13.8	3,613	100,000	657	16.0	0.589	0.196	0.0812	674	0.186	0.67
Treatment Group 3 (F-PF-03814927 + PF-03409397/45)												
Pre-Application	LGJ-6	12.4	3,371	0	ND	ND	ND	Not sampled		--	--	--
	DOI-6	8.2	2,576	0	ND	0.0551	ND	Not sampled		--	--	--
	CQI-6	8.7	2,677	0	ND	ND	ND	Not sampled		--	--	--
	BEK-0	6.9	2,303	0	<LOQ	ND	ND	Not sampled		--	--	--
	PLI-6	10.3	2,988	0	<LOQ	ND	ND	Not sampled		--	--	--
4 hours	LGJ-6	12.4	3,371	100,000	2,722	27.67	1.90	0.779	0.196	2,753	0.817	2.75
	DOI-6	8.2	2,576	100,000	2,633	15.7	1.62	0.556	0.262	2,651	1.03	2.65
	CQI-6	8.7	2,677	100,000	3,856	35.6	1.97	0.313	0.0847	3,893	1.45	3.89
	BEK-0	6.9	2,303	50,000	1,367	16.7	2.07	0.316	0.0646	1,386	0.602	2.77
	PLI-6	10.3	2,988	100,000	3,000	89.0	13.9	1.90	0.462	3,105	1.04	3.11

Table 8. Fipronil Residues from Cotton Gloves Following 20 Contact Simulations to Treated Dogs[1]

Interval	Animal #	Animal Weight (kg)	Animal Surface Area (cm^2)	Actual Dose Applied (µg ai)	Measured Residue on Gloves (µg/glove)[2, 3]					Total Residue		% of applied dose transferred[6]
					Outer Cotton Glove #1	Inner Cotton Glove #2	Inner Cotton Glove #3	Inner Cotton Glove #4	Inner Cotton Glove #5	µg/gloves[4]	µg/cm^2 surface area of dog[5]	
Day 1	LGJ-6	12.4	3,371	100,000	1,644	22.3	1.82	0.280	0.112	1,669	0.495	1.67
	DOI-6	8.2	2,576	100,000	1,967	18.9	1.97	0.767	0.686	1,989	0.772	1.99
	CQI-6	8.7	2,677	100,000	1,867	43.2	4.09	1.029	0.189	1,915	0.715	1.92
	BEK-0	6.9	2,303	50,000	936	23.7	1.56	0.369	0.039	961	0.417	1.92
	PLI-6	10.3	2,988	100,000	2,322	46.7	4.20	0.682	0.140	2,374	0.795	2.37
Day 2	LGJ-6	12.4	3,371	100,000	992	18.9	2.50	1.12	0.342	1,015	0.301	1.02
	DOI-6	8.2	2,576	100,000	1,222	16.3	2.29	0.832	0.960	1,243	0.482	1.24
	CQI-6	8.7	2,677	100,000	812	10.9	1.47	0.307	0.0916	825	0.308	0.82
	BEK-0	6.9	2,303	50,000	439	13.2	1.12	0.267	0.0592	454	0.197	0.91
	PLI-6	10.3	2,988	100,000	1,722	26.2	2.16	1.38	0.739	1,753	0.587	1.75
Day 4	LGJ-6	12.4	3,371	100,000	1,049	18.2	2.96	0.780	0.337	1,071	0.318	1.07
	DOI-6	8.2	2,576	100,000	1,289	18.0	1.72	0.886	0.207	1,310	0.508	1.31
	CQI-6	8.7	2,677	100,000	489	11.9	0.916	0.946	0.144	503	0.188	0.50
	BEK-0	6.9	2,303	50,000	433	7.0	0.850	0.112	0.0376	441	0.192	0.88
	PLI-6	10.3	2,988	100,000	1,489	50.9	9.43	1.34	0.513	1,551	0.519	1.55
Day 7	LGJ-6	12.4	3,371	100,000	692	14.1	2.70	0.587	0.113	710	0.211	0.71
	DOI-6	8.2	2,576	100,000	1,378	14.6	2.00	0.442	0.452	1,395	0.542	1.40
	CQI-6	8.7	2,677	100,000	376	8.80	0.880	0.230	0.101	386	0.144	0.39
	BEK-0	6.9	2,303	50,000	369	5.73	0.453	0.0843	0.076	375	0.163	0.75
	PLI-6	10.3	2,988	100,000	1,589	28.7	3.16	0.566	0.647	1,622	0.543	1.62

1. **Nominal application rates were :**
   20 mg of demiditraz/kg and 6.7 mg of fipronil/kg bw for Treatment Groups 1 and 2
   10 mg of demiditraz/kg bw and 6.7 mg of fipronil/kg bw for Treatment Group 3.
2. Residues were corrected for field fortification recovery using the average percent recovery from the fortification level closest to the field residue.
   Treatment Group 1: 89% for residues <5,005 µg/sample and 97% for residues ≥5,005 µg/sample
   Treatment Group 2: 95% for residues <5,005 µg/sample and 94% for residues ≥5,005 µg/sample
   Treatment Group 3: 90% for residues <5,005 µg/sample and 95% for residues ≥5,005 µg/sample
3. LOQ = 0.03 µg/glove. ND = Not detected (no peak). LOD was not provided. When residues were reported as less than the LOQ or ND, Versar used a value of ½ LOQ (0.015 µg/glove) in the calculations.
4. Total Residue (µg/gloves) = outer cotton glove #1 + inner glove #2 + inner glove #3 (µg/glove) + inner glove #4 (µg/glove) + inner glove #5 (µg/glove).
5. Total Residue (µg/cm^2) = Total residue on all 5 gloves / cm^2 body surface area of the dog.
6. % of applied dose transferred = Total Residue (µg/gloves) / applied dose (µg ai) *100

Note: One simulation = 60 strokes

Table 9. Summary of Demiditraz Residues from Cotton Gloves Following 20 Contact Simulations to Treated Dogs[1]

Interval	n	Total Residue[2]						% of applied dose transferred[5]		
		µg/gloves[3]			µg/cm^2 body surface area of dog[4]					
		Range	Average	Standard Deviation	Range	Average	Standard Deviation	Range	Average	Standard Deviation
Treatment Group 1 (F/PF-03814927 + PF-03409397/18)										
4 hours	5	5,591-10,725	7,764	2,039	2.51-4.13	2.989	0.66	2.72-4.07	3.37	0.61
1 day		3,833-6,616	5,131	1,273	1.70-2.55	1.966	0.33	1.74-2.58	2.22	0.36
2 days		1,997-7,017	3,869	2,045	0.884-2.70	1.463	0.72	1.18-2.34	1.57	0.45
4 days		890-4,835	2,504	1,880	0.394-1.64	0.917	0.60	0.401-1.61	0.983	0.52
7 days		725-2,857	1,679	1,027	0.321-1.10	0.620	0.33	0.450-0.95	0.660	0.24
Treatment Group 2 (F/PF-03814927 + PF-03409397/05)										
4 hours	5	5,264-8,780	7,533	1373	1.46-3.08	2.61	0.68	1.75-2.93	2.51	0.46
1 day		2,171-3,859	2,604	709	0.637-1.35	0.893	0.273	0.724-1.29	0.868	0.24
2 days		1,170-3,870	2,190	1087	0.324-1.36	0.762	0.403	0.390-1.29	0.730	0.36
4 days		1,782-3,196	2,357	563	0.583-1.12	0.808	0.225	0.594-1.065	0.786	0.19
7 days		1,831-2,383	2,051	221	0.589-0.87	0.700	0.106	0.610-0.794	0.684	0.07
Treatment Group 3 (F-PF-03814927 + PF-03409397/45)										
4 hours	5	2,409-6,923	4,973	1,645	1.05-2.59	1.785	0.59	3.18-4.62	3.64	0.59
1 day		1,671-4,002	3,037	864	0.726-1.35	1.087	0.27	1.98-2.67	2.25	0.27
2 days		656-3,109	1,647	919	0.285-1.04	0.584	0.30	0.870-2.07	1.19	0.52
4 days		306-1,198	768	393	0.133-0.417	0.272	0.13	0.280-0.798	0.55	0.21
7 days		266-1,336	704	471	0.115-0.447	0.251	0.16	0.222-0.891	0.50	0.28

1. **Nominal application rates were:**
   20 mg of demiditraz/kg and 6.7 mg of fipronil/kg bw for Treatment Groups 1 and 2
   10 mg of demiditraz/kg bw and 6.7 mg of fipronil/kg bw for Treatment Group 3.
2. Residues were corrected for field fortification recovery.
3. Total Residue (µg/gloves) = outer cotton glove #1 + inner glove #2 + inner glove #3 (µg/glove) + inner glove #4 (µg/glove) + inner glove #5 (µg/glove).
4. Total Residue (µg/cm^2) = Total residue on all 5 gloves / cm^2 body surface area of the dog.
5. % of applied dose transferred = Total Residue (µg/gloves) / applied dose (µg ai) *100

Table 10. Summary of Fipronil Residues from Cotton Gloves Following 20 Contact Simulations to Treated Dogs[1]

Interval	n	Total Residue (Corrected) [2]						% of applied dose transferred[5]		
		µg/gloves[3]			µg/cm^2 body surface area of dog[4]					
		Range	Average	Standard Deviation	Range	Average	Standard Deviation	Range	Average	Standard Deviation
Treatment Group 1 (F/PF-03814927 + PF-03409397/18)										
4 hours	5	1,726-3,283	2,340	616	0.741-1.26	0.903	0.21	2.41-3.70	3.06	0.60
1 day		1,377-2,208	1,716	353	0.585-0.850	0.662	0.11	1.70-2.78	2.27	0.49
2 days		823-2,682	1,455	756	0.364-1.03	0.554	0.27	1.20-2.68	1.80	0.55
4 days		451-1,681	953	637	0.174-0.647	0.354	0.21	0.48-1.68	1.15	0.50
7 days		264-1,087	639	407	0.117-0.419	0.235	0.13	0.50-1.09	0.75	0.30
Treatment Group 2 (F/PF-03814927 + PF-03409397/05)										
4 hours	5	1,439-2,599	2,214	450	0.398-0.911	0.769	0.21	1.44-2.60	2.21	0.45
1 day		674-2,257	1,350	574	0.186-0.791	0.471	0.22	0.67-2.26	1.35	0.57
2 days		675-2,427	1,365	682	0.187-0.850	0.476	0.25	0.68-2.43	1.37	0.68
4 days		671-1,301	895	249	0.204-0.456	0.308	0.10	0.67-1.30	0.90	0.25
7 days		674-914	772	92	0.186-0.334	0.266	0.05	0.67-0.91	0.77	0.09
Treatment Group 3 (F-PF-03814927 + PF-03409397/45)										
4 hours	5	1,386-3,893	2,758	909	0.602-1.45	0.988	0.32	2.65-3.89	3.03	0.51
1 day		961-2,374	1,782	524	0.417-0.795	0.639	0.17	1.67-2.37	1.97	0.25
2 days		454-1,753	1,058	484	0.197-0.587	0.375	0.16	0.82-1.75	1.15	0.37
4 days		441-1,551	975	490	0.188-0.519	0.345	0.16	0.50-1.55	1.06	0.40
7 days		375-1,622	898	579	0.144-0.543	0.320	0.20	0.39-1.62	0.97	0.52

1. **Nominal application rates were 20 mg of demiditraz/kg and 6.7 mg of fipronil/kg bw for Treatment Groups 1 and 2, and 10 mg of demiditraz/kg bw and 6.7 mg of fipronil/kg bw for Treatment Group 3.**
2. Residues were corrected for field fortification recovery.
3. Total Residue (µg/gloves) = outer cotton glove #1 + inner glove #2 + inner glove #3 (µg/glove) + inner glove #4 (µg/glove) + inner glove #5 (µg/glove).
4. Total Residue (µg/cm^2) = Total residue on all 5 gloves / cm^2 body surface area of the dog.
5. % of applied dose transferred = Total Residue (µg/gloves) / applied dose (µg ai) *100

Table 11. Regression Summary for % of Application Rate Transferred to Gloves Following 20 Contact Simulations to Treated Dogs

Statistic	Treatment Group 1	Treatment Group 2	Treatment Group 3
Demiditraz			
Actual Average Day 0 (% of applied dose transferred)	3.37	Not appropriate R^2 value extremely low	3.64
Predicted Day 0 (% of applied dose transferred)	2.81		2.75
Slope	-0.238		-0.306
Half-life (days)	2.9		2.3
R^2	0.733		0.727
Fipronil			
Actual Average Day 0 (% of applied dose transferred)	3.06	Not appropriate R^2 value extremely low	Not appropriate R^2 value extremely low
Predicted Day 0 (% of applied dose transferred)	2.79		
Slope	0.210		
Half-life (days)	3.3		
R^2	0.721		

Figure 1. Graph of % of Applied Dose Transferred vs Time for Demiditraz

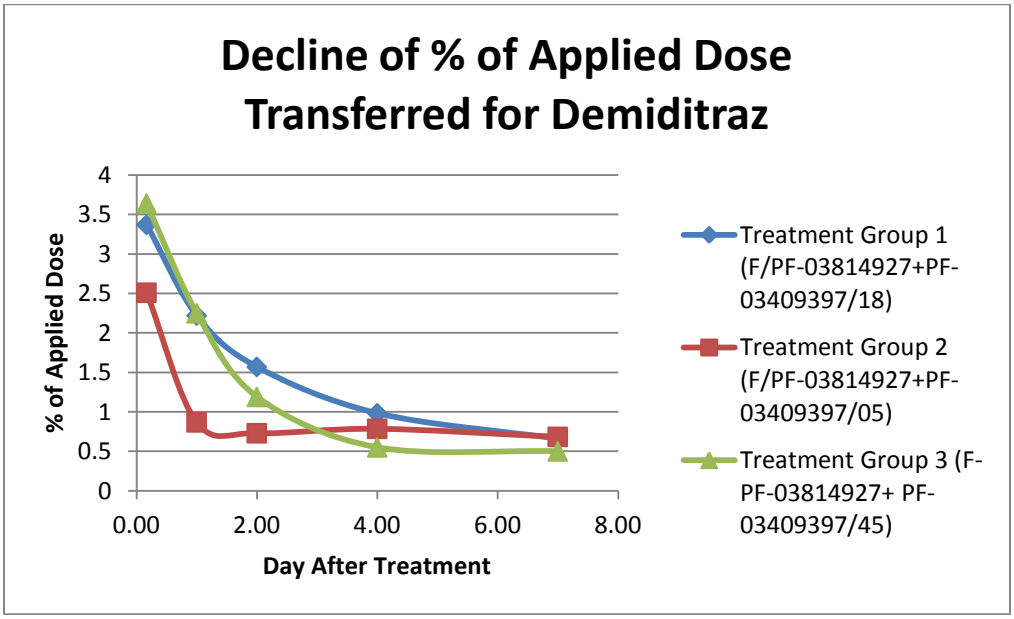
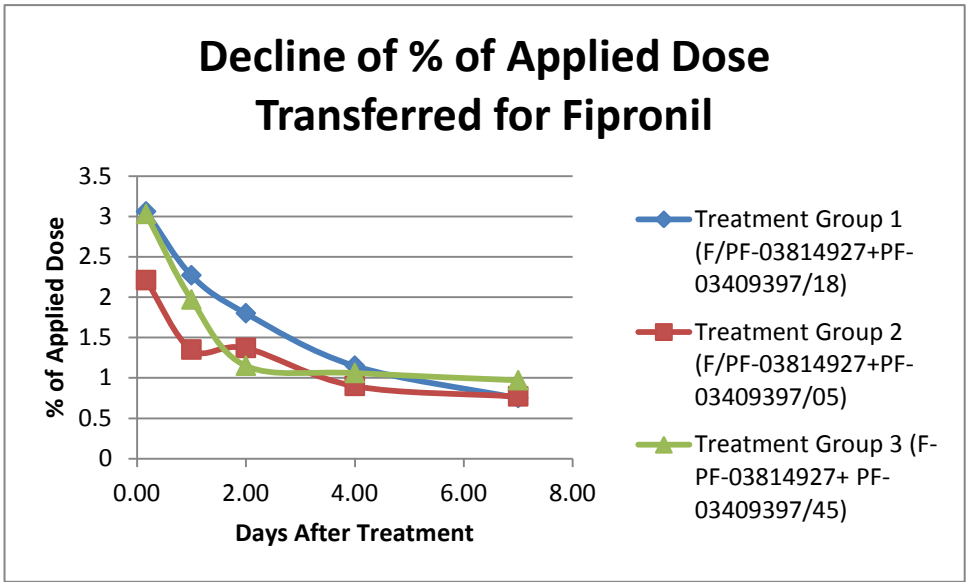


Figure 2. Graph of % of Applied Dose Transferred vs Time for Fipronil



Appendix A

Compliance Checklist

COMPLIANCE CHECKLIST

This compliance checklist is based on applicable criteria of the OPPTS Test Guidelines Series 875, Occupational and Residential Exposure Test Guidelines, Group B: 875.2300 (indoor surface residue) and OPPTS Test Guidelines Series 875, Occupational and Residential Exposure Test Guidelines, Group B: 875.2400 (dermal exposure).

1. *The test substance must be the typical end use product of the active ingredient.* This criterion was met.

2. *The production of metabolites, breakdown products, or the presence of contaminants of potential toxicological concern, should be considered on a case-by-case basis.* This criterion was not met. Samples were analyzed for demiditraz and fipronil only and no discussion of production of metabolites or breakdown products was provided.

3. *Indoor surface residue studies should be conducted under ambient conditions similar to those encountered during the intended use season, and should represent reasonable worst case conditions.* This criterion was met.

4. *Ambient conditions (i.e., temperature, barometric pressure, ventilation) should be monitored.* This criterion was met.

5. The *end use product should be applied by the application method recommended on the label.* This criterion appears to have been met. According to the Study Report, applications were made based on the intended label instructions.

6. *The application rate used in the study should be provided and should be the maximum rate specified on the label. However, monitoring following application at a typical application rate is more appropriate in certain cases.* All dogs received the appropriate intended label recommended rate.

7. *If multiple applications are made, the minimum allowable interval between applications should be used.* This criterion does not apply. Only one application was made.

8. *Indoor surface residue (ISR) data should be collected from several different types of media (e.g., carpeting, hard surface flooring, counter tops, or other relevant materials).* This criterion was met; however, only one breed of dog was monitored.

9. *Sampling should be sufficient to characterize the dissipation mechanisms of the compound (e.g., three half-lives or 72 hours after application, unless the compound has been found to fully dissipate in less time; for more persistent pesticides, longer sampling periods may be necessary). Sampling intervals may be relatively short in the beginning and lengthen as the study progresses. Background samples should be collected before application of the test substance occurs.* This criterion was met. Samples were collected for up to 7 days after application at which time residues were extremely low.

10. *Triplicate, randomly collected samples should be collected at each sampling interval for each surface type.* This criterion was met. Five replicates were collected at each sampling interval for each treatment group.

11. *Samples should be collected using a suitable methodology (e.g., California Cloth Roller,*

Polyurethane Roller, Drag Sled, Coupons, Wipe Samples, Hand Press, vacuum cleaners for dust and debris, etc.) for indoor surfaces. This criterion appears to be met. Samples were collected using cotton and nitrile gloves over a mannequin hand. Each sample consisted of 20 contact simulations with three strokes per simulation. The sample collection method followed the US EPA Science Advisory Council for Exposure Draft Guidance Document for Development of Protocols to Collect Pet Fur Transferable Residues Using Mannequin Hands, dated January 2011.

12. *Samples should be stored in a manner that will minimize deterioration and loss of analytes between collection and analysis. Information on storage stability should be provided.* This criterion was partially met. Samples were stored frozen between sample collection and analysis. A storage stability study was not conducted; however, field fortification was conducted to demonstrate the stability of residues.

13. *Validated analytical methods of sufficient sensitivity are needed. Information on method efficiency (residue recovery), and limit of quantitation (LOQ) should be provided.* This criterion was met. A validated LOQ was provided.

14. *Information on recovery samples must be included in the Study Report. A complete set of field recoveries should consist of at least one blank control sample and three or more each of a low-level and high-level fortification. These fortifications should be in the range of anticipated residue levels in the field study.* This criterion was partially met. Field fortification was conducted using two levels. The innermost glove demonstrated levels which were less than the lowest field fortification level for the inner glove samples.

15. *Raw residue data must be corrected if appropriate recovery values are less than 120 percent.* This criterion was not met. Residues were not corrected for field fortification recoveries.

16. *The monitoring period should be of sufficient duration to result in reasonable detectability on dosimeters. Monitoring should be conducted before residues have dissipated beyond the limit of quantification. Baseline samples should be collected before the exposure activity commences.* These criteria were met. Baseline samples were collected prior to treating the dogs. Residues of demiditraz and fipronil were <LOQ in all samples except for two samples, in which demiditraz was detected at 0.0366 ppm (Treatment Group III, Animal #BEK-0, Glove 1) and fipronil was detected at 0.0551 ppm (Treatment Group III, Animal #DOI-6, Glove 2).

17. *Activities monitored must be clearly defined and representative of typical practice.* This criterion was partially met. The activity of stroking a dog is a typical post-application activity; however, other activities may compose typical behavior with a companion animal (e.g., hugging).

18. *Sufficient control samples should be collected.* This criterion was met. Control samples were collected from all dogs prior to treatment.

Appendix B

Regressions

Regression Analysis: Summary Output for Demiditraz Treatment Group 1

Regression Statistics	
Multiple R	0.85622
R Square	0.733114
Adjusted R^2	0.72151
Standard Error	0.366272
Observations	25

ANOVA

	df	*SS*	*MS*	*F*	*Signif. F*
Regression	1	8.475766	8.475766	63.178957	4.79072E-08
Residual	23	3.085562	0.134155		
Total	24	11.56133			

	Coeff.	*Std. Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*
Intercept	1.03472	0.112128	9.228036	3.404E-09	0.802765809	1.266674103
Slope	-0.23815	0.029961	-7.94852	4.791E-08	-0.300129507	-0.176169393

Half Life = 2.910555 Days

Predicted Concentration Levels

Time (Days)	Residue (% of Applied Dose Transferred)
0	2.814318
1	2.217922
2	1.74791
3	1.377502
4	1.085588
5	0.855536
6	0.674235
7	0.531354
8	0.418752
9	0.330012
10	0.260078
11	0.204963
12	0.161529
13	0.127298
14	0.100322
15	0.079062
16	0.062308
17	0.049104
18	0.038698

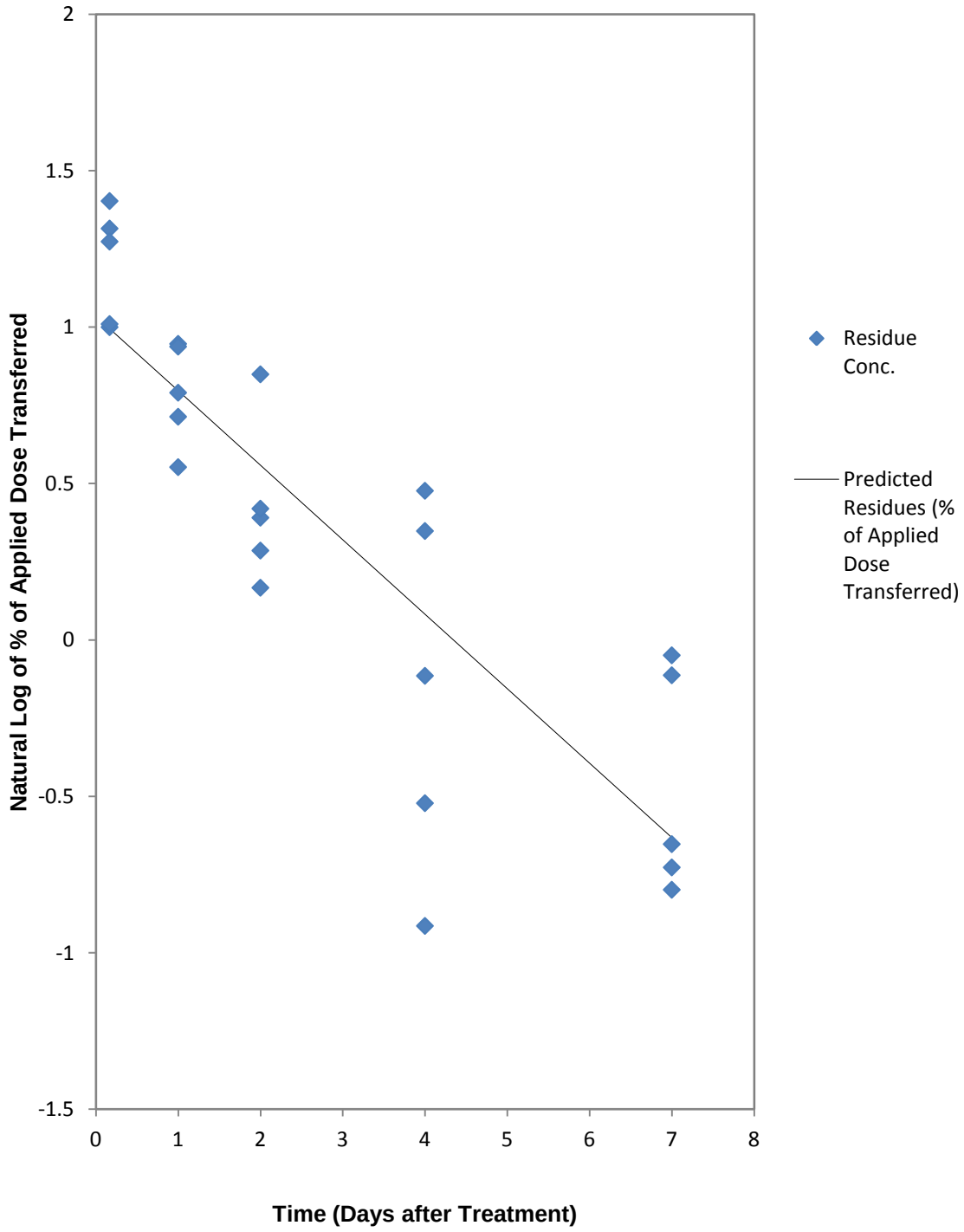
Time (Days)	Residue (% of Applied Dose Transferred)
21	0.0189411
22	0.0149272
23	0.0117639
24	0.009271
25	0.0073063
26	0.005758
27	0.0045378
28	0.0035762
29	0.0028183
30	0.0022211
31	0.0017504
32	0.0013795
33	0.0010871
34	0.0008568
35	0.0006752

19	0.030497
20	0.024034

Regression Analysis: Means and CVs for Demiditraz Treatment Group 1

Days after Last Treatment	Residues (% of Applied Dose Transferred)	Mean (% of Applied Dose Transferred)	Standard Deviation (% of Applied Dose Transferred)	Coefficient of Variation (%)
0.17	3.73	3.37	0.607	18
	2.72			
	4.07			
	3.58			
	2.75			
1	2.58	2.22	0.355	16
	2.04			
	2.56			
	2.21			
	1.74			
2	1.48	1.57	0.45	28.6
	1.52			
	1.33			
	2.34			
	1.18			
4	0.89	0.983	0.52	52.9
	1.61			
	0.59			
	1.42			
	0.40			
7	0.52	0.66	0.242	36.7
	0.89			
	0.48			
	0.95			
	0.45			

Regression Analysis: Log of % of Applied Dose Transferred vs. Time for Demiditraz Treatment Group 1



Regression Analysis: Summary Output for Demiditraz Treatment Group 3

Regression Statistics	
Multiple R	0.85267
R Square	0.727046
Adjusted R^2	0.715178
Standard Error	0.477252
Observations	25

ANOVA

	df	*SS*	*MS*	*F*	*Signif. F*
Regression	1	13.9539	13.9539	61.263193	6.22728E-08
Residual	23	5.238702	0.22777		
Total	24	19.1926			

	Coeff.	*Std. Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*
Intercept	1.009927	0.146103	6.912447	4.78E-07	0.707690619	1.312163479
Slope	-0.30557	0.03904	-7.82708	6.227E-08	-0.386328039	-0.224807916

Half Life = 2.268389 Days

Predicted Concentration Levels

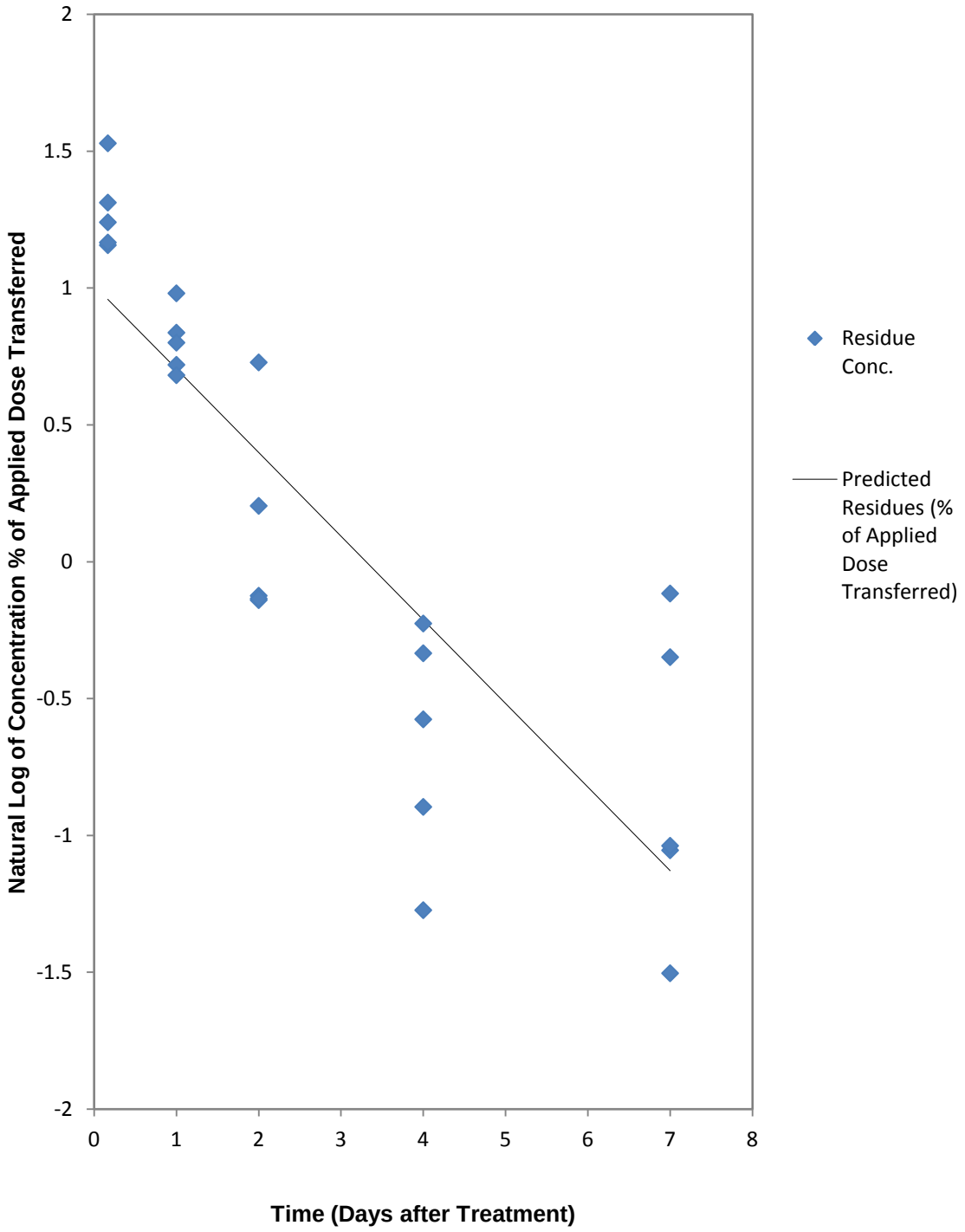
Time (Days)	Residue (% of Applied Dose Transferred)
0	2.745401
1	2.02255
2	1.490022
3	1.097707
4	0.808686
5	0.595763
6	0.438901
7	0.323341
8	0.238207
9	0.175488
10	0.129283
11	0.095243
12	0.070166
13	0.051692
14	0.038082
15	0.028055
16	0.020668
17	0.015226
18	0.011217
19	0.008264
20	0.006088

Time (Days)	Residue (% of Applied Dose Transferred)
21	0.0044851
22	0.0033042
23	0.0024342
24	0.0017933
25	0.0013211
26	0.0009733
27	0.000717
28	0.0005282
29	0.0003892
30	0.0002867
31	0.0002112
32	0.0001556
33	0.0001146
34	8.445E-05
35	6.221E-05

Regression Analysis: Means and CVs for Demiditraz Treatment Group 3

Days after Last Treatment	Residues (% of Applied Dose Transferred)	Mean (% of Applied Dose Transferred)	Standard Deviation (% of Applied Dose Transferred)	Coefficient of Variation (%)
0.17	3.18	3.64	0.588	16.2
	3.46			
	4.62			
	3.21			
	3.72			
1	2.05	2.25	0.27	12
	2.31			
	1.98			
	2.23			
	2.67			
2	0.88	1.19	0.519	43.6
	1.23			
	0.87			
	0.87			
	2.07			
4	0.56	0.553	0.213	38.6
	0.72			
	0.28			
	0.41			
	0.80			
7	0.35	0.504	0.281	55.8
	0.71			
	0.22			
	0.35			
	0.89			

Regression Analysis: Log of % of Applied Dose Transferred vs. Time for Demiditraz Treatment Group 3



Regression Analysis: Summary Output for Fipronil Treatment Group 1

Regression Statistics	
Multiple R	0.849258
R Square	0.721239
Adjusted R^2	0.709119
Standard Error	0.332466
Observations	25

ANOVA

	df	*SS*	*MS*	*F*	*Signif. F*
Regression	1	6.577634	6.577634	59.507913	7.96153E-08
Residual	23	2.542277	0.110534		
Total	24	9.11991			

	Coeff.	*Std. Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*
Intercept	1.025166	0.101779	10.07248	6.67E-10	0.814620076	1.235711477
Slope	-0.20979	0.027196	-7.71414	7.962E-08	-0.266054456	-0.153535369

Half Life = 3.303928 Days

Predicted Concentration Levels

Time (Days)	Residue (% of Applied Dose Transferred)
0	2.787558
1	2.260014
2	1.832307
3	1.485544
4	1.204406
5	0.976472
6	0.791675
7	0.641851
8	0.520381
9	0.421899
10	0.342055
11	0.277321
12	0.224838
13	0.182288
14	0.14779
15	0.119821
16	0.097145
17	0.07876
18	0.063855

Time (Days)	Residue (% of Applied Dose Transferred)
21	0.0340295
22	0.0275894
23	0.0223681
24	0.018135
25	0.014703
26	0.0119204
27	0.0096645
28	0.0078355
29	0.0063526
30	0.0051504
31	0.0041757
32	0.0033854
33	0.0027447
34	0.0022253
35	0.0018042

19	0.05177
20	0.041973

Regression Analysis: Means and CVs for Fipronil Treatment Group 1

Days after Last Treatment	Residues (% of Applied Dose Transferred)	Mean (% of Applied Dose Transferred)	Standard Deviation (% of Applied Dose Transferred)	Coefficient of Variation (%)
0.17	3.70	3.06	0.599	19.6
	2.41			
	3.45			
	3.28			
	2.43			
1	2.75	2.27	0.488	21.5
	1.90			
	2.78			
	2.21			
	1.70			
2	1.85	1.8	0.546	30.3
	1.65			
	1.65			
	2.68			
	1.20			
4	1.06	1.15	0.503	43.8
	1.62			
	0.90			
	1.68			
	0.48			
7	0.57	0.749	0.297	39.7
	1.06			
	0.53			
	1.09			
	0.50			

Regression Analysis: Log of Concentration vs. Time for Fipronil Treatment Group 1